REMARKS

Amendments to the Claims

Applicants have amended Claims 9, 54, 55, and 58, as noted above.

Applicants have amended Claim 9 to delete the term "hydroxy compound" and to substitute therefor the phrase "hydroxy-functional compound of an aliphatic or acyclic saturated or unsaturated hydrocarbon, a phenol, or polyphenol" to describe the component compound specified in step (b)(ii) of the claimed process. According to the invention, the component compound of step(b)(ii) of Claim 9, as amended herein, is one of two elements (the other is specified in step (b)(i)) that are present during the step of immobilization of nucleic acid to the non-siliceous surface (first specified in step (a) of Claim 9). The amendment reinstates descriptive language that was previously recited in Claim 9 (see, e.g., Claim 9 in Applicants' Responses dated December 21, 2001 and September 12, 2002) and in original Claims 54, 55, 57, 58, and 65, without objection. Similarly, Applicants have amended Claims 54, 55, and 58 to conform the language of these claims with the description of the component compound of step (b)(ii) of Claim 9, as amended herein. Accordingly, the amendments add no new matter, but ensure consistent use of terms throughout the claims as provided by the original disclosure.

Entry of the amendments and reconsideration of the claims are respectfully requested.

Regarding objections to "hydroxy compound" and "hydroxyl derivatives"

The Examiner objected to the term "hydroxy compound", as previously recited in Claims 9 and 58, and to the term "hydroxyl derivatives", as previously recited in Claim 54. In particular, the Examiner considered the terms "new matter" not found in the specification and requiring cancellation. With the view that the objected to terms present new matter, the Examiner also rejected Claims 9-13, 20, 37-56, 58-75, 113-116, and 121-129 as based on a specification that does not comply with the written description requirement and that lacks an enabling disclosure of the claimed invention under 35 USC § 112, first paragraph. Applicants request reconsideration of the objections for the reasons discussed below.

As noted above, Applicants have amended Claims 9, 54, 55, and 58 to eliminate recitation of the aforementioned terms objected to by the Examiner and to replace those terms with the descriptive language previously recited in the claims and the original disclosure without

objection, e.g., in original Claims 54, 55, and 57 and in a prior versions of Claim 9 (see, Applicants' Responses dated December 21, 2001 and September 12, 2002). As amended, Claims 54, 55, and 58 recite language that is consistent with the amendment to Claim 9 made herein.

Applicants submit that the amendments to Claims 9, 54, 55, and 58 (and, thereby, claims depending therefrom) render the Examiner's objections moot. Accordingly, reconsideration and withdrawal of the rejections of the claims are respectfully requested.

Regarding Rejections under 35 USC § 102(b)/103(a)

In the Office Action of August 12, 2003, the Examiner has rejected Claims 9-13, 20, 37-56, 58-75, 113-116, 121-129, as anticipated by or, in the alternative, obvious over U.S. Patent No. 4,798,789 ("Lee"). For the reasons provided below, Applicants respectfully traverse the rejection.

With respect to Lee, the Examiner notes:

> "13. Lee et al., column 7, disclose a method of isolating mRNA from a sample whereby a chaotropic agent is used. The mRNA is bound to oligo-dT cellulose. ***The presence of cellulose is considered to meet the requirement that a hydroxyl compound is present as well as the requirement that the nucleic acid sample be applied to a 'non-siliceous surface.'***
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> "14. Lee et al., columns 13-14, disclose the isolation of DNA from cells and the reversible immobilization of the nucleic acid to a cellulose column. Column 14 teaches that the immobilization and washes were performed with a buffer that was at 0° C. Elution was effected by the introduction of 'water at room temperature.' ***The aspect of having the DNA reversibly immobilized on a cellulose column meets the requirement that the sample be brought into contact with a non-siliceous surface, and that the sample be in contact with a hydroxy compound (the cellulose resin).*** The presence of sodium chloride meets the requirement that a salt of a metal be present.
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> "15. Column 14 discloses performing additional steps on the released DNA, e.g., precipitation and digestion as well as additional extraction steps where phenol was used. Such disclosures meet a limitation of claim 20.

> "16. The presence of NaCl in the buffer meets a limitation of claims 46-48 in that a sodium halide is present." (pp. 5-6 of the Office Action; emphasis added).

According to paragraphs 13 and 14 of the above excerpt of the Office Action, a key feature of the Examiner's reliance on Lee is the view that an oligo(dT) or oligo(dA) cellulose affinity resin used in Lee to isolate a target nucleic acid by complementary base pairing could play the role of a non-siliceous surface in Applicants' claimed process in Claim 9 as well as serve as another element of the invention, i.e., as the component compound now specified in step (b)(ii) of Claim 9, as amended herein.

Applicants respectfully submit that the Examiner has interpreted Applicants' claimed invention in a manner that is inconsistent with both the plain language of the claims, as amended herein, and the clear description of the claimed process provided by Applicants' specification. In particular, Applicants submit that Claim 9, as amended herein, clearly recites an element that is a non-siliceous surface to which a nucleic acid sample is applied according to step (a) and that this non-siliceous surface is a separate and distinct element from either of two other elements, i.e., the component compounds specified in step (b)(i) and (ii), respectively. Furthermore, the plain language of Claim 9 clearly requires that the component compounds specified in step (b)(i) and (ii) must be present during the step of reversibly immobilizing nucleic acids to the non-siliceous surface element. Thus, these three elements of Claim 9, as amended herein, are distinct and separable from one another, and no basis is provided in the claims for "merging" any of these three elements with one another or for assuming that any one of these elements may substitute for another.

Furthermore, claims are read and understood in light of the specification. See, e.g., *All Dental Prodx, LLC v. Advantage Dental Products, Inc.*, 309 F.3d 774, 780, 64 USPQ2d (BNA) 1945, 1949 (Fed. Cir. 2002); *Markman v. Westview Instruments Inc.*, 52 F.3d 967, 979, 343 USPQ3d (BNA) 1321, 1329 (Fed. Cir. 1995). A person of ordinary skill in this art who reads Applicants' specification would readily appreciate the physically separate and distinct nature of the non-siliceous surface first mentioned in step (a) of Claim 9 and each of the component compounds specified in step (b) (i) and (ii), which are present during the immobilization of nucleic acids to the non-siliceous surface. In fact, descriptions of each of these three elements of the claimed process of the invention may be found in separate, consecutive sections of the

specification. Thus, a description of the component compound specified in step (b)(i) may be found at p. 17, line 1-p. 18, line 5, of the specification; a description of the component compound of step (b)(ii) may be found at p. 18, lines 6-13, of the specification; and a description of various surfaces (including membrane surfaces) to which nucleic acids may be applied to, immobilized on, and eluted from, according to Applicants' invention may be found at p. 18, line 19-p. 20, line 12, of the specification. Moreover, the specification also contains a variety of working examples of carrying out the claimed process by employing representative species of each of these three elements specified in Claim 9, as amended herein (see, e.g., Examples 1-30, pp. 30-62 of the specification). Nowhere in any of the working examples of the specification is there any teaching or suggestion that a non-siliceous surface may also substitute for either of the component compounds (as specified in step (b)(i) and (ii) of Claim 9, as amended herein) for immobilization of the nucleic acids to that non-siliceous surface.

Clearly, the process in Lee and the process of Applicants' invention of Claim 9, as amended herein, necessarily employ different elements for carrying out different processes. Lee describes a standard protocol of using oligonucleotide cellulose affinity resins to isolate homologous polynucleotides by complementary base pairing (i.e., hybridization, annealing) between known sequences of the desired target nucleic acid molecule and known sequences of the oligonucleotide resin, e.g., polyA-mRNA complementary base pairing to an oligo(dT) cellulose column (see, Lee at column 7, lines 45-51) or dT-tailed DNA complementary base pairing to an oligo(dA) cellulose column (see, Lee at column 14, lines 17-21). The processes of Lee necessarily employs the elements of a targeted nucleic acids (to be isolated) that has at least a partially known sequence and an oligonucleotide affinity resin having a known nucleotide sequence that is complementary to the known sequence of the target nucleic acid to be isolated. Absent these two elements having known complementary nucleotide sequences, there is no isolation process according to Lee. In contrast, Applicants' claimed invention provides a process for isolating nucleic acids on a non-siliceous surface that is not based on complementary base pairing between homologous nucleic acid molecules and, thus, is not restricted to, does not require, and does not recite a target nucleic acid to be isolated having a known nucleotide sequence and a "non-siliceous surface" having an oligonucleotide sequence that is known to be complementary to the sequence of a target nucleic acid to be isolated. ***To reiterate, a distinguishing feature and advantage of Applicants' claimed invention over Lee is that no***

sequence information is required to isolate a nucleic acid according to Applicants' invention, whereas the affinity protocols described in Lee can only work when a nucleic acid molecule carries a known nucleotide sequence that is necessarily complementary to the particular oligonucleotide of the affinity resin. Thus, Lee not only recites different elements than those in Applicants' claimed invention, but ***lacks*** the above-mentioned three elements employed in Applicants' claimed process according to Claim 9, as amended herein.

For anticipation under 35 USC § 102 by a reference, that reference must teach each and every element or aspect of the claimed invention. As explained in § 2131 of the Manual of Patent Examining Procedure (MPEP):

> **"TO ANTICIPATE A CLAIM, THE REFERENCE MUST TEACH EVERY ELEMENT OF THE CLAIM**
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> " 'A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.' *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). 'The identical invention must be shown in as complete detail as is contained in the . . . claim.' *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989)." (emphasis in original).

Lee clearly does not describe how to isolate any nucleic acid in the absence of actual knowledge of its nucleotide sequence and how to employ the three separate elements recited in Claim 9, as amended herein, to carry out such an isolation according to Applicants' claimed invention. Accordingly, Lee does not teach each and every element of Applicants' claimed invention and therefore does not anticipate the claims, as amended herein, under 35 USC § 102(b). The Examiner is, therefore, respectfully requested to reconsider and withdrawn the rejection under 35 USC § 102(b).

As explained above, Lee describes a protocol for using an oligonucleotide affinity column for isolating nucleic acids based on annealing (hybridization) of complementary nucleotide base sequences of homologous nucleic acid strands, i.e., of the oligonucleotide resin and of the sought after target nucleic acid, whereas, Applicants' claimed invention does not employ and does not teach or suggest a process based on complementary base pairing between an oligonucleotide affinity resin of known sequence and a target nucleic acid of at least partially

known sequence. Thus, Lee does not teach or suggest Applicants' process for isolating nucleic acid without knowledge of the nucleic acid's nucleotide sequence.

Moreover, it appears that only by first reading Applicants' disclosure does the Examiner find the necessity to transmute the complementary oligonucleotide affinity resin of Lee into ***two*** of the several elements employed in the claimed process of Applicants' invention to render Applicants' claims obvious. However, the Examiner's reasoning is improper and contrary to knowledge of persons of ordinary skill in this art at the time of Applicants' invention. ***Lee*** provides no teaching, motivation, or suggestion to be viewed as Applicants' own invention for isolating nucleic acids without sequence information. Absent guidance in the prior art, the Patent Office is forbidden from so modifying a prior art reference so as to arrive at Applicants' invention and, thereby, reject a claim to the invention as obvious:

> "A critical step in analyzing the patentability of claims pursuant to section 103(a) is casting the mind back to the time of invention, to consider the thinking of one of ordinary skill in the art, ***guided only by the prior art references and the then-accepted wisdom in the field***. *See, Dembiczak*, 175 F.3d at 999, 50 USPQ2d at 1617. Close adherence to this methodology is especially important in cases where the very ease with which the invention can be understood may prompt one 'to fall victim to the insidious effect of a hindsight syndrome wherein that which only the invention taught is used against its teacher.' *Id.* (quoting *W.L. Gore & Assoc., Inc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 USPQ 303, 313 (Fed. Cir. 1983)).
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> "Even when obviousness is based on a single prior art reference, there must be a showing of a suggestion or motivation to modify the teachings ***of that reference***. *See, B.F. Goodrich Co. v. Aircraft Breaking Sys. Corp.*, 72 F.3d 1577, 1582, 37 USPQ2d 1314, 1318 (Fed. Cir. 1996)."

In re Kotzab, 217 F.3d 1365, 1369-70, 55 USPQ2d 1313, 1316-17 (Fed. Cir. 2000) (emphasis added).

Casting the mind back to the time of Applicants' invention, a person of ordinary skill in the art would be expected to have known of Lee's description of a standard method of isolating target nucleic acids of at least partially known nucleotide sequence by complementary base

pairing (annealing) with a known sequence of an oligonucleotide affinity resin. However, Lee lacks any teaching or suggestion of isolating nucleic acids by a method that does not employ complementary base pairing elements and, particularly, of Applicants' claimed invention that provides isolation of ***any*** nucleic acid molecule regardless of its nucleotide sequence, without an oligonucleotide affinity resin of known nucleotide sequence, but rather, comprising use of the three elements of a non-siliceous surface as first recited in step (a) of amended Claim 9, a component compound as specified in step (b)(i) of amended Claim 9, and a component compound as specified in step (b)(ii) of amended Claim 9.

The above discussion clearly shows that Lee fails to teach or suggest Applicants' invention as recited in Claim 9, as amended herein. Moreover, as Lee does not teach or suggest Applicants' process as recited in Claim 9, the rejections of other claims depending from Claim 9, including *inter alia* Claims 20 and 46-48, also must fall. Accordingly, Applicants respectfully request that the Examiner reconsider and withdraw the rejections under 35 USC § 103(a).

Conclusion

The above comments and amendments to the claims clearly show that Applicants' claimed invention is fully supported by the specification and that Lee does not teach or suggest Applicants' claimed invention for isolating nucleic acids. Accordingly, Applicants submit that the claims, as amended herein, are now in condition for allowance and respectfully request that the Examiner enter the amendments, withdraw the rejections, and pass the present application to issue.

The amendments made to the claims herein render the rejections of the Office Action moot, making it unnecessary for Applicants to address the rejections on the merits. The amendments to the claims are not intended to signify and should not be interpreted to signify acquiescence or agreement with the rejections, and the amendments to the claims do not evidence any intention on the part of Applicants to abandon inventive subject matter encompassed by the original claims and excluded by the amended claims.

The Examiner is respectfully encouraged to contact Applicants' undersigned attorneys by telephone to discuss any additional matters with respect to advancing this case to allowance and grant of Letters Patent.

Respectfully submitted,

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December 11, 2003
Date

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